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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/715,270 | 11/14/2003 | Lynne Ann Krummen | P1937R1 | 4580 |

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| EXAMINER | |
|---|---|
| GUIDRY, GUY L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/715,270 | KRUMMEN ET AL. | |
| | Examiner | Art Unit | |
| | Guy Guidry, Ph.D. | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *30 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *21-84* is/are pending in the application.

4a) Of the above claim(s) *21-35,38,40-56 and 80* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36,37,39,57-79 and 81-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/6/2006*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *¶20060720* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Receipt of a response filed on 30 January 2006 to the Restriction/Election mailed on 30 December 2005 is acknowledged. Claims 1-20 are cancelled. New claims 57-84 have been entered. Claims 21-84 are pending in this application. It is noted that in the previous Office Action (mailed 4/19/2006) certain claims were inadvertently omitted from consideration. While new claims 57-80, 82-84 were filed after the December 2005 Requirement for Restriction was mailed and before the First Action on the Merits, they are considered to be properly grouped with claims 36, 37 and 39 with respect to the antecedent restriction requirements. Therefore, claims 36, 37, 39, 57-79, 81-84 are under consideration in this Action.

### *Election/Restrictions*

Applicant's election **without traverse** of Group III, claims 36, 37 and 39 in the reply filed on 30 January 2006 is acknowledged. Claims 21-35, 38 and 40-56 and 80 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking. New claims 57-80, 82-84 are rejoined with claims 36, 37, and 39, all of which are under consideration in the Action.

### *Priority*

Applicants' claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied

with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/426,095 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The provisional application does not provide a written description for the limitation of claims 36, 37, 39, 57-70, 73 and 74 wherein the cloned host cell is capable of producing 250 mg/L of the product of interest. Accordingly, claims 36, 37, 39, 57-70, 73 and 74 are not entitled to the benefit of the prior application.

***Claim Objections***

Claim 37 objected to because of the following informalities: the claim contains two acronyms CHO and DHFR that are presented without definition. Inclusion of the full name of Chinese hamster ovary (CHO) and dihydrofolate reductase (DHFR) would be remedial for this claim.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 36, 37, 39, 57-70, 73 and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Claims 36, 37, 39, 57-70, 73 and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The claims are drawn to a host cell wherein the cell is capable of producing at least about 250 mg/L of the product of interest. Without parameters further defining production, it is not clear what type of production Applicants intend to claim. For example, one interpretation to the limitation "producing at least about 250 mg/L of the product of interest" is that one cell may produce that amount over the lifetime of the cell. Another interpretation is that at least about 250 mg is excreted and contained in 1L of the culture media at some point in time. Still another interpretation is that a batch culture system, including all product of interest within the cells and that secreted into the media, contains at least about 250 mg/L of the product of interest. Further, the claim is drawn to a host cell *capable* of producing at least about 250 mg/L, wherein the nature of the recited liter is not defined. Given broadest possible interpretation, essentially all cells have such a capacity because a dilute solution of the product of interest may be sufficiently concentrated so that a concentration of 250 mg/L of the product of interest is obtained. For example, a cell culture supernatant containing

25 mg/L of the product of interest concentrated10 fold produces a 250 mg/L solution containing the product of interest produced by the host cell. Without further definition, the claim is indefinite.

Claim 37 recites the limitation "the CHO cell" of claim 36. There is insufficient antecedent basis for this limitation in the claim.

Claims 39 and 57-70 are further rejected as being indefinite because the claims are drawn to a composition comprising a host cell of claim 36. As written, it is not clear whether the host cell of claim 36 is of the population of cells selected for transfection, one of a population cultured in a selective medium or a cloned cell from the selected cell population.

The term "splicing efficiency" in claim 58 is a relative term which renders the claim indefinite. The term "splicing efficiency" with respect to a range of percentages is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, splicing efficiency could be affected by factors such as temperature or salt composition of the solution in which the splicing occurs, and such parameters are not defined.

Claim 65 recites “the selectable gene” of claim 57. There is insufficient antecedent basis for this limitation in the claim.

Claims 72 and 75 recite the limitation "the host cell population" of claim 71. It is not clear whether Applicant intends to culture or place in a spinner vessel the host cell

population of claim 71 prior to the introduction of a DNA construct or the host cell that contains the DNA construct. The different interpretations of the claim limitation lead to materially distinct products, rendering the claims indefinite.

Claim 73 recites "the selected host cell population" of claim 72. There is insufficient antecedent basis for this limitation in the claim.

Claim 84 is indefinite for reciting steps (b) and (c), where (b) and (c) refer to parts of a DNA construct product and not a process step. A person of skill in the art would not be able to interpret such contradictory limitations in any precise way, therefore the claim is indefinite.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

**Claims 36, 37, 39, 57-70, 73 and 74 are rejected under 35 U.S.C. 102(b) as being anticipated by Chisholm et al., (WO 01/04306 A1, 18 January 2001, of record), hereinafter the '306 reference.**

The claims have been give broadest possible interpretation. The limitation of claim 58 wherein the clamed intron provides a splicing efficiency of between 80% and 99% is considered indefinite as described above, but is interpreted here to mean such a splicing efficiency could be obtained under optimized conditions, with the addition of any factors necessary to obtain said optimization. Regarding the limitations of claim 75-77, which recite that the host cell population is in a spinner vessel or at specific densities, it is noted that the limitations are recited in the process of making the claimed host cell. Determination of the patentability of a product-by-process claim is based on the identity of the product, not its method of production. If the product in the product-by-process claim is the same (or obvious) from a product of the prior art, the claim is unpatentable, even if the product was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). When assessing patentability, the product-by-process claim has potential patentability when the manufacturing steps impart identifiable, distinctive structural characteristic to the final product. In the instant case, there is no evidence to suggest that introducing the DNA construct into a population of host cells in a spinner vessel or at a given density would impart identifiable, distinctive structural characteristics on the final product. Therefore, absent evidence to the contrary, the claimed product is anticipated by the art.

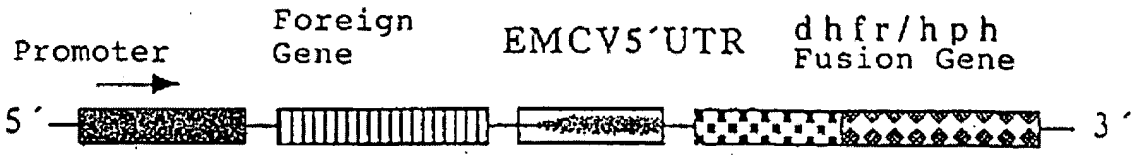
The '306 reference teaches vectors containing a transcription regulatory region comprising an SV40 promoter (or alternatively a CMV promoter, p. 16, ¶1), a fusion gene comprising a selectable gene and an amplifiable gene comprising puromycin/DHFR fusion gene (where the puromycin gene is 5' to the DHFR gene) positioned within an intron between the transcriptional regulatory region (promoter) and the gene encoding a product of interest (see especially Fig. 16), either 52196His or 332222His or a humanized antibody, (see especially Examples2, 3 and 4, pp. 39-42), (the vector may contain two transcription units and two introns (p. 4, ¶¶4-5)) transfection into CHO cells or NIH-3T3 cells (both mammalian) with a DHFR-phenotype (see especially p. 33, l. 34) culturing the host cell in a selective medium containing puromycin or methotrexate (concentration of methotrexate may range from 1nM to 1000nM, p. 30, ¶4) (Examples 3 and 4, and p. 34, ¶2). Since the vector construct containing an amplifiable marker and DHFR- CHO cells are operationally the same in the '306 reference and the instant application, the host cell of the '306 reference is presumably capable of producing 250 mg/L of the product of interest and cell culture cell density of at least about $5X10^5$/ml and $1.5X10^5$/ml. The Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562

F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2 d 1922, 1923 (BPAI 1989). Therefore, claims 36, 37, 39, 57-70, 73 and 74 are fully anticipated by WO 01/04306 A1.

**Claims 36, 39, 57, 59, 61-64, 68, 71-78, 81-83 are rejected under 35 U.S.C. 102(b) as anticipated by Herlitschka et al. (US Patent 6,114,146, of record; hereinafter the '146 patent).**

The claims have been given broadest possible interpretation. The '146 patent teaches expression vectors, transformed cells and methods of utilizing the same to produce foreign proteins in said transformed cells, wherein the expression vector contains a dicistronic transcription unit. (e.g., Abstract). More particularly, the '146 patent teaches a vector (i.e., polynucleotide) comprising a promoter (the promoter may be a CMV promoter, see especially Example 1, construction of vectors), a foreign gene (i.e., selected sequence encoding a desired product) and a fusion gene comprising a first selectable gene and an amplifiable gene as is depicted in Figure 1:

FIG. 1




As the figure demonstrates, DHFR is fused with *hph* which is gene encoding an antibiotic selectable protein (i.e., hygromycin B phosphotransferase; claims 59-64, 66

and 115) (col. 14, l. 65). The fusion gene may me considered to be positioned within an intron defined by 5' splice donor and 3' splice acceptor sites of poor quality 9see figure 1 above). The reference further teaches that an example of a foreign gene is human factor VIII, which meets the limitation of a product of interest such as a hormone (e.g., Factor VIII binds a host of cellular factors, such as lipoprotein receptor-related protein). (e.g., col. 6, last ¶; claim 80) or may be a plasma protein (e.g. humanized antibody)(col. 6, ¶11).

The '146 patent teaches that the expression vectors can be utilized to transform CHO cells (col. 5, ll. 1-8, ll. 15-31; col. 9, ll. 10-17; claims 84-87), particularly DHFR deficient CHO cells (col. 5, l. 15) in methotrexate (10nM to 100nM, col. 12, ¶9). Further, the expression vectors can contain a CMV or SV40 promoter. (col. 6, ll. 3-6). As the system is highly similar to that claimed in the instant application, the host cell presumable would have the capacity to produce 250 mg/L of the product interest, meeting the production limitation of claims 36 and 39. The Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2 d

1922, 1923 (BPAI 1989). Therefore, claim 36 and 39 are fully anticipated by US 6,114,146.

Claim 36, 37, 39, 57-79, 81-84 are rejected under 35 U.S.C. 102(e) as being anticipated by US Application 10/714,000, (US PGPUB 2005/0005310) which claims priority of US Provisional Application 60/143,360.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The reasons for this rejection are similar to those presented in the rejection presented above, over WO 01/04306. To summarize, US 10/714,000 discloses a host cell producing a product of interest comprising introducing a DNA construct comprising a transcriptional regulatory region, a fusion gene comprising a selectable gene and an amplifiable gene and a gene encoding a product of interest (see especially all of the Figures, for examples of various gene constructs), culturing the cell and cloning a cell (producing at least 250 mg of product of interest- which is considered an ill defined process limitation which may be optimized through routine experimentation). The amplifiable gene can be DHFR, the selectable gene puromycin and the cell may be DHFR defective. The fusion gene may be positioned within an intron (see especially

Fig. 3). Methotrexate concentration may vary and may include a chimeric protein. The reference contemplates protein of interest may be a humanized antibody. Various host cells are contemplated in the reference application, including XHO cells. The host cell may further comprise a second transcriptional regulatory region and a second gene encoding a second protein of interest, encompassing the various embodiments as presented for a gene construct and host cell described above. Various promoters are contemplated, including SV40 and CMV.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**Claim 36, 37, and 39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 85, 86, 87, 88 and 91 of copending Application No. 10/714,000.**

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reference claims are

directed to a host cell, a CHO cell with a DHFR- phenotype wherein the cells are transformed with polynucleotides comprising in operable linkage, a fusion gene comprising a first selectable gene and an amplifiable second gene wherein the amplifiable gene is the gene encoding DHFR and the selectable gene is the gene encoding puromycin resistance, a selected sequence encoding a product of interest and a promoter. Reference claim 91 is drawn to a method of culturing the cell to produce the product of interest, anticipating the cell culture composition of instant claim 39. Therefore, the reference claims fully anticipate the instant rejected claims.

The U.S. Patent and Trademark Office normally will not institute interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 10/714,000, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Guy Guidry, Ph.D. whose telephone number is 571-272-7928. The examiner can normally be reached on Monday through Friday 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the

problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Guy Guidry, Ph.D.

Examiner

Art Unit 1636

DANIEL M. SULLIVAN
PATENT EXAMINER